



### CLAIMS

The invention in which an exclusive right is asserted is claimed as follows:

1. A method for minimizing the aggregation tendencies of an amyloid forming protein,  
the method comprising:
  - a) identifying a first amino acid sequence of the protein that is replaced by a second amino acid sequence during physiological conditions; and
  - b) preventing the replacement by juxtaposing a peptide to the first amino acid sequence.
2. The method as recited in claim 1 wherein the method is conducted *in vivo*.
3. The method as recited in claim 1 wherein the protein is a human protein selected from the group consisting of human kappa-IV light chain variable domain and serine protease inhibitors.
4. The method as recited in claim 3 wherein the peptide has an amino acid sequence identical to an amino acid sequence in a region of the light chain variable domain.
5. The method as recited in claim 3 wherein the peptide is inserted between residue position numbers 60 and 83 of the protein.

1           6.     The method as recited in claim 3 wherein the peptide has the amino acid sequence  
 2                               Phe<sub>71</sub>-Thr<sub>72</sub>-Leu<sub>73</sub>-Thr<sub>74</sub>-Ile<sub>75</sub>-Ser<sub>76</sub>-Ser<sub>77</sub>  
 3     and wherein the subscripts denote the positions of the amino acids in the domain.

1           7.     The method as recited in claim 1 wherein the peptide is inserted when the protein is  
 2     partially unfolded.

1           8.     The method as recited in claim 1 wherein the peptide is identical in composition to a  
 2     portion of the protein that anchors a hairpin-shaped amino acid sequence to the protein.

1           9.     The method as recited in claim 1 wherein the protein is a greek key fold protein  
 2     selected from the group consisting of antibody constant domains, transthyretin, beta-2-microglobulin,  
 3     serine protease inhibitors, and crystalline.

1           10.    The method as recited in claim 9 wherein the peptide is inserted at a hairpin anchorage  
 2     point in the greek key fold protein.

1           11.    The method as recited in claim 1 wherein the peptide is a target for an endoplasmic  
 2     reticulum chaperone.

sub  
 A2 1           12.    The method as recited in claim 1 wherein the peptide is an endoplasmic reticulum  
 2     chaperone selected from the group consisting of hsp70, hsc73 and BiP.

1           13.    The method as recited in claim 1 wherein the peptide is a synthetic peptide selected  
 2     from the group consisting of TDFTLTI, FTLTISS, FTLKISR, FTLEISR, and LTLKLSR.

1           14.    A peptide for insertion in an intact human kappa-IV light chain variable domain, the  
2 peptide comprising the following amino acid sequence:

3                               Phe<sub>71</sub>-Thr<sub>72</sub>-Leu<sub>73</sub>-Thr<sub>74</sub>-Ile<sub>75</sub>-Ser<sub>76</sub>-Ser<sub>77</sub>

4           wherein the subscript numbers are the residue location points in the domain.

1           15.    A method for preventing amyloid formation in human kappa-IV light chain variable  
2 domain, the method comprising inserting the peptide Phe<sub>71</sub>-Thr<sub>72</sub>-Leu<sub>73</sub>-Thr<sub>74</sub>-Ile<sub>75</sub>-Ser<sub>76</sub>-Ser<sub>77</sub> into the  
3 domain, wherein the subscript numbers indicate the residue location on the domain.

1           16.    The method as recited in claim 15 wherein the domain is partially unfolded at the time  
2 of insertion.

1           17.    A method for preventing fibril assembly, the method comprising:  
2                   a)    identifying a region of a first aggregating protein moiety that normally interacts  
3 with a second protein moiety to form the assembly; and  
4                   b)    juxtaposing a binding protein to the first moiety.

1           18.    The method as recited in claim 17 wherein the first and second aggregating proteins  
2 are immunoglobulin light chains.

1           19.    The method as recited in claim 17 wherein the binding protein hybridizes with the  
2 region.

1           20.    The method as recited in claim 17 wherein the binding protein is an amino acid  
2 sequence that is complementary to the amino acid sequence of the region.